

PATENT
Docket No.: 28069-585-DIV
(Formerly: 003301-072)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Nils Ove Gustavsson *et al.* Confirmation No.: 3614
Serial No. : 10/627,920 Customer No. : 35437
Filed : July 28, 2003
Art Unit : 1623
Examiner : Krishnan, Ganapathy
For : **Pharmaceutically Acceptable Starch**

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION OF RICHARD E. JONES UNDER 37 C.F.R. §1.132

I, Richard E. Jones, Ph.D., declare and state that:

1. I am Senior Vice President of Research and Development at SkyePharma, Inc., San Diego, CA. I have held this position for almost three years. I earned my Ph.D. degree in physical chemistry from Stanford University and have had over thirty years' experience in the design and development of pharmaceutical products, particularly in the areas of formulation design and characterization, and excipient (inactive ingredient) characterization. As Senior VP of R&D at SkyePharma, I am responsible for directing formulation design, process research and development, analytical research and development, and nonclinical development (including toxicology) activities.

2 I have reviewed and understand the above-identified patent application, the Advisory Action, dated June 6, 2005 and the Examiner's comments stated therein. In the Advisory Action, the Examiner remarks that the a comparison of the starches in the claims of the instant application and in the co-pending patent application U.S. Serial No. 10/461,393, filed on June 16, 2003, "shows that the characteristics like molecular weight ranges, purity levels and

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dissolution characteristics in water are identical. The mode of molecular weight reduction is not seen to render the starch claimed in either application patentably distinct”.

3. I have made a prior declaration in the instant application. In the prior declaration, based on my knowledge and experience in the area of starch formulations and methodology, I set forth distinctions between a starch product whose molecular weight is reduced by shearing versus a starch product whose molecular weight is reduced by acid hydrolysis. As stated in my prior declaration, a starch product produced by acid hydrolysis is distinct and different in terms of molecular weight distribution and other qualities from a starch product produced by shearing.

4. Further to my prior declaration, I am making this declaration to provide the results of experiments that unequivocally demonstrate the differences in both the molecular weight distribution and the size attributes of starch products that result from a shearing process versus an acid hydrolysis process used to reduce the molecular weight of amylopectin starch comprising the starch compositions.

5. The starch starting materials used in the experiments were essentially as described in the instant application (e.g., on pages 11-17 and Examples 1 and 2) and in co-pending patent application U.S. Serial No. 10/461,393. (e.g., on pages 12-17 and Example 1). The process of acid hydrolyzing the amylopectin starch to reduce the molecular weight was performed as described in application U.S. Serial No. 10/461,393, for example, on pages 18-19 and Example 2. The process of shearing the amylopectin starch to reduce the molecular weight was performed as described in the instant application, for example, on pages 17-22 and Examples 1 and 2. Samples of the resulting acid-hydrolyzed and sheared starch were analyzed by high pressure liquid chromatography (HPLC) with detection by multi-angle light scattering. Graphs were generated to display the results of the HPLC analysis of the two types of starch products.

6. The results of the HPLC analysis as described in ¶5 are presented in the two graphs attached hereto at Tabs 1 and 2.

6a. In the graph shown at Tab 1, cumulative weight fraction is plotted versus molecular weight for the acid-hydrolyzed starch material and the sheared starch material. In this graph, the red line represents acid-hydrolyzed starch and the blue line represents sheared starch. As can be observed from the results presented in this graph, the acid-hydrolyzed starch comprises a generally lower molecular weight species than does the sheared starch, as well as a broader molecular weight distribution.

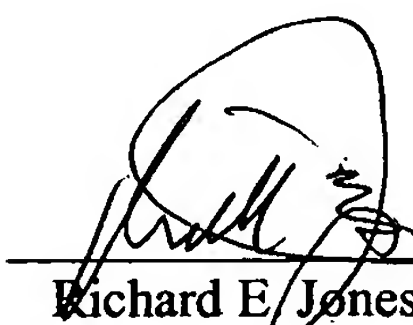
6b. In the graph shown at Tab 2, the same data are plotted as weight fraction versus molecular weight for the acid-hydrolyzed starch material and the sheared starch material. In this graph, the red line represents acid-hydrolyzed starch and the blue line represents sheared starch. As can be observed from the results presented in this graph, the acid-hydrolyzed starch displays a much broader molecular weight distribution compared with that of the sheared starch, as well as a generally lower molecular weight.

7. Based on the results obtained from the experiments described herein, the use of shearing to reduce the molecular weight of the starch is demonstrated to yield a starch that exhibits a more narrow molecular weight distribution, within a molecular weight range, compared with the use of acid hydrolysis to reduce the molecular weight of the starch. As can be seen from the graphs, acid-hydrolyzed starch has a more disperse molecular weight distribution within a molecular weight range, e.g., a 10 to 10,000 kDa molecular weight range, while sheared starch has a more narrow molecular weight distribution within the range. (Tab 2). The graph at Tab 2 demonstrates that a starch product produced by shearing is distinct and different from a starch product produced by acid hydrolysis, since the molecular weight distribution of the starch fragments produced by shearing is demonstrably different from the molecular weight distribution of starch fragments produced by acid hydrolysis. Further, it can also be observed that acid-hydrolyzed starch is comprised of a generally lower molecular weight species than is sheared starch. (Tab 1).

8. Based on my knowledge and experience in the field, and on the results of the analyses described herein, a starch product comprising amylopectin that is subjected to molecular weight reduction by acid hydrolysis is technically and discernibly different from a starch product comprising amylopectin that has been subjected to molecular weight reduction by shearing. Thus, the two types of starch products are not the same and do not overlap.

I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. §1001 and that willful false statements may jeopardize the validity of this patent application and any patent issuing thereon.

Dated: 22 July 05

Signed: 
Richard E. Jones, Ph.D.

